



NATIONAL PBM BULLETIN

May 14, 2007

**DEPARTMENT OF VETERANS AFFAIRS
VETERANS HEALTH ADMINISTRATION
PHARMACY BENEFITS MANAGEMENT STRATEGIC HEALTHCARE GROUP,
MEDICAL ADVISORY PANEL, OFFICE OF THE CHIEF CONSULTANT FOR OPHTHALMOLOGY AND
CENTER FOR MEDICATION SAFETY (VA MEDSAFE)
Pergolide withdrawal from the market**

I. ISSUE – Development of valvulopathy in patients receiving pergolide therapy

II. BACKGROUND –

On March 29, 2007 The U.S. Food and Drug Administration (FDA) announced that manufacturers of pergolide drug products, which are used to treat Parkinson's disease, will voluntarily remove these drugs from the market because of the risk of serious damage to patients' heart valves.

The products being withdrawn are Permax, the trade name for pergolide marketed by Valeant Pharmaceuticals, and two generic versions of pergolide manufactured by Par and Teva. Pergolide is in a class of medications called dopamine agonists and is used with levodopa and carbidopa to manage the symptoms (tremors and slowness of movement) of Parkinson's disease.

III. DISCUSSION - REVIEW OF WARNING

In 2006, a boxed warning regarding the risk of serious heart valve damage was added to the labeling for pergolide.

Two recent New England Journal of Medicine studies confirm previous findings associating pergolide with increased chance of regurgitation (backflow of blood) of the mitral, tricuspid, and aortic valves of the heart. Valve regurgitation is a condition in which valves don't close tightly, allowing blood to flow backward across the valve. Symptoms include shortness of breath, fatigue and heart palpitations.

In light of this additional post-market safety information, the companies that manufacture and sell pergolide will stop shipping pergolide for distribution and, in cooperation with FDA, will withdraw the products from the market.

There are alternative agents from the dopamine agonist class available to treatment for Parkinson's disease that do not have comparable safety problems, the companies that manufacture and sell pergolide have stopped shipping pergolide for distribution and will, in cooperation with FDA, work to remove from the market both the name brand Permax (pergolide) and the generic versions of pergolide. The effect of this voluntary withdrawal on supplies of pergolide currently in pharmacies will not be immediate. This delay will allow time for healthcare professionals and patients to discuss appropriate treatment options and to change treatments.

IV. VA MEDSAFE RECOMMENDATIONS

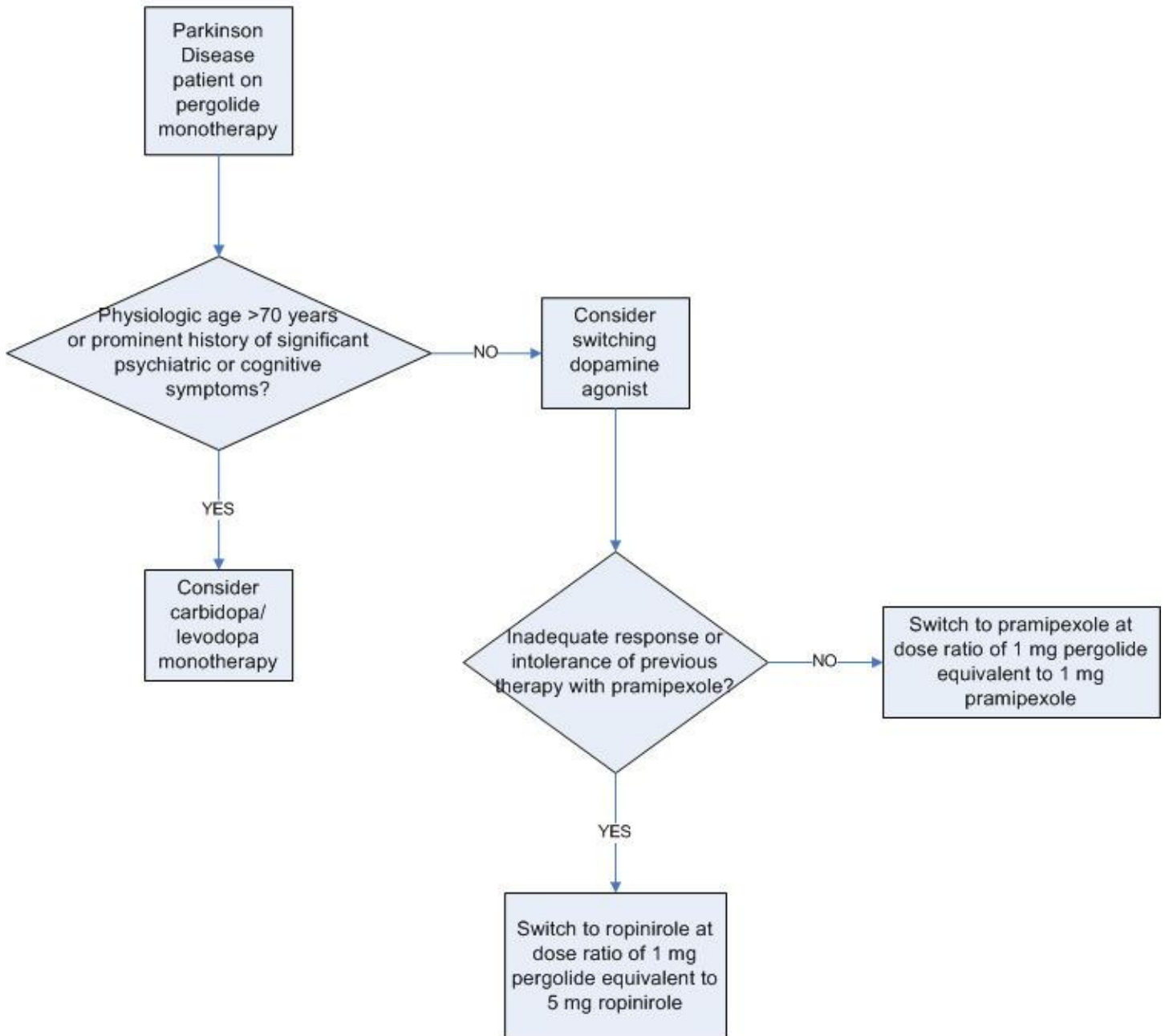
Healthcare professionals who prescribe pergolide should consider the following:

- Assess the patient's need for dopamine agonist (DA) therapy. If continued treatment with a DA is necessary, another DA should be substituted for pergolide. There are other dopamine agonists approved for the treatment of Parkinson's disease that are not associated with heart valve damage. Published transition regimens describe the conversion from one DA to another.
- If treatment with a DA is to be discontinued, **pergolide should not be stopped abruptly**, because rapid discontinuation of all dopamine agonist therapies can be dangerous. Instead, gradually decrease the dose of pergolide.
- Patients who will be taken off pergolide should be told that other effective options for treatment exist, including three other DAs that are not associated with damage to heart valves.

V. REFERENCES

1. Dewey RB 2nd, Reimold SC, O'Suilleabhain PE. Cardiac valve regurgitation with pergolide compared with nonergot agonists in Parkinson disease. *Arch Neurol*. 2007 Mar;64(3):377-80.
2. Zanettini R, Antonini A, Gatto G, Gentile R, Tesei S, Pezzoli G. Valvular heart disease and the use of dopamine agonists for Parkinson's disease. *N Engl J Med*. 2007 Jan 4;356(1):39-46.
3. Schade R, Andersohn F, Suissa S, Haverkamp W, Garbe E. Dopamine agonists and the risk of cardiac-valve regurgitation. *N Engl J Med*. 2007 Jan 4;356(1):29-38.
4. Junghanns S, Fuhrmann JT, Simonis G, Oelwein C, Koch R, et al. Valvular heart disease in Parkinson's disease patients treated with dopamine agonists: a reader-blinded monocenter echocardiography study. *Mov Disord*. 2007 Jan 15;22(2):234-8.
5. Yamamoto M, Uesugi T, Nakayama T. Dopamine agonists and cardiac valvulopathy in Parkinson disease: a case-control study. *Neurology*. 2006 Oct 10;67(7):1225-9.
6. Kim JY, Chung EJ, Park SW, Lee WY. Valvular heart disease in Parkinson's disease treated with ergot derivative dopamine agonists. *Mov Disord*. 2006 Aug;21(8):1261-4.
7. Peralta C, Wolf E, Alber H, Seppi K, Muller S, et al. Valvular heart disease in Parkinson's disease vs. controls: An echocardiographic study. *Mov Disord*. 2006 Aug;21(8):1109-13.
8. Scozzafava J, Takahashi J, Johnston W, Puttagunta L, Martin WR. Valvular heart disease in pergolide-treated Parkinson's disease. *Can J Neurol Sci*. 2006 Feb;33(1):111-3.
9. Zadikoff C, Rochon P, Lang A. Cardiac valvulopathy associated with pergolide use. *Can J Neurol Sci*. 2006 Feb;33(1):27-33.
10. Waller EA, Kaplan J, Heckman MG. Valvular heart disease in patients taking pergolide. *Mayo Clin Proc*. 2005 Aug;80(8):1016-20.
11. Horvath J, Fross RD, Kleiner-Fisman G, Lerch R, Stalder H, et al. Severe multivalvular heart disease: a new complication of the ergot derivative dopamine agonists. *Mov Disord*. 2004 Jun;19(6):656-62.
12. Van Camp G, Flamez A, Cosyns B, Weytjens C, Muyldermans L, et al. Treatment of Parkinson's disease with pergolide and relation to restrictive valvular heart disease. *Lancet*. 2004 Apr 10;363(9416):1179-83.

Conversion of Parkinson's Disease patient on pergolide monotherapy



Conversion of Parkinson's Disease patient on pergolide adjunct therapy with carbidopa/levodopa

